

AD _____

GRANT NUMBER: DAMD17-94-J-4466

TITLE: Molecular Biology of Breast Neoplasia

PRINCIPAL INVESTIGATOR: Christopher A. Bradfield, Ph.D.

CONTRACTING ORGANIZATION: Northwestern University Medical School
Chicago, Illinois 60611

REPORT DATE: October 1995

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for public release;
distribution unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

19960520 104

DATA QUALITY INSPECTED 1

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.

1. AGENCY USE ONLY (Leave blank)		2. REPORT DATE October 1995		3. REPORT TYPE AND DATES COVERED Annual 23 Sep 94 - 22 Sep 95	
4. TITLE AND SUBTITLE Molecular Biology of Breast Neoplasia				5. FUNDING NUMBERS DAMD17-94-J-4466	
6. AUTHOR(S) Christopher A. Bradfield, Ph.D.					
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Northwestern University Medical School Chicago, Illinois 60611				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012				10. SPONSORING / MONITORING AGENCY REPORT NUMBER	
11. SUPPLEMENTARY NOTES					
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for public release; distribution unlimited				12b. DISTRIBUTION CODE	
13. ABSTRACT (Maximum 200 words) The Robert H. Lurie Cancer Center is an NCI-designated (5P30 CA60553) multi-disciplinary clinical and research center. The Cancer Center has significant strengths in the area of breast cancer, both in basic and clinical research. The training grant, "Molecular Biology of Breast Neoplasia" enables 4 pre-doctoral students per year to be exposed to the latest concepts in the biology, diagnosis and treatment of breast cancer. Four students were selected in October 1994, and four new students were selected in October 1995. These students are in an ideal position to maximize research efforts and pursue careers in breast cancer research that may impact on the disease. The Cancer Center just received supplemental funds for one post-doctoral position per year for the next three years of the training grant. This will further expand the pool of highly qualified candidates in the field of breast cancer biology to hopefully develop new strategies in the treatment and prevention of breast cancer.					
14. SUBJECT TERMS training grant; breast; neoplasia breast cancer				15. NUMBER OF PAGES 21	
				16. PRICE CODE	
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unlimited		

FOREWORD

Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the US Army.

Where copyrighted material is quoted, permission has been obtained to use such material.

Where material from documents designated for limited distribution is quoted, permission has been obtained to use the material.

Citations of commercial organizations and trade names in this report do not constitute an official Department of Army endorsement or approval of the products or services of these organizations.

CB In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Resources, National Research Council (NIH Publication No. 86-23, Revised 1985).

For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.

CB In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

CB In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

CB In the conduct of research involving hazardous organisms, the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.

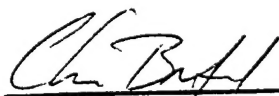

PI - Signature 10/11/95 Date

TABLE OF CONTENTS

<u>Title</u>	<u>Page</u>
Front Cover	1
SF 298 Report Documentation	2
Foreword	3
Table of Contents	4
Introduction	5
Body	5
Conclusions	11
Appendix	13-21

INTRODUCTION

The Northwestern University Robert H. Lurie Cancer Center is an NCI-designated (5P30 CA60553-03) multi-disciplinary clinical and laboratory research center, integrating the expertise and resources of the Medical School and its five affiliated hospitals along with those of the basic science departments located on the Evanston Campus. The Cancer Center is dedicated to excellence in research, prevention, diagnosis, treatment and rehabilitation, as well as to the education of scientists, health professionals and the public. The Cancer Center promotes the advancement of clinical and basic research, and provides an environment that encourages the rapid application of new technology to patient care. The affiliated hospitals treat a combined total of 5,000 cancer patients each year.

The Cancer Center has extended significant resources toward establishing a premier breast cancer program at Northwestern. In October 1993 Dr. V. Craig Jordan, a world renowned breast cancer researcher was recruited as Director of Breast Cancer Research. Dr. Monica Morrow, a leading breast cancer surgeon, was also recruited to direct the clinical program at Northwestern. Dr. Morrow directs the Lynn Sage Comprehensive Breast Center at Northwestern, established with private philanthropy funds. The Center has state-of-the-art mammography facilities, education and medical exam facilities. In February 1994 the Lurie Cancer Center (Drs. Jordan and Morrow) successfully competed for a breast cancer program planning grant from the National Cancer Institute (NCI # 1P20 CA 65764-01). In addition, investigators have received two interactive RO1's focused on hormonal and nutritional aspects in breast cancer prevention, an R21 targeting breast cancer therapeutics and angiogenesis, and three Illinois Department of Public Health Breast Cancer Research Grants on breast cancer prevention, early detection and translational research.

BODY

In September, 1994, the Lurie Cancer Center received funding from the Department of Defense to implement a training program in breast cancer biology entitled, "The Molecular Biology of Breast Neoplasia". The objective of the program is to establish a predoctoral training program with a focus on breast cancer research. This program enables students to be exposed to an outstanding basic science faculty with research interests relevant to breast cancer and a highly regarded clinical faculty who can translate this research to the clinic. The basic goal of the program is to provide a sound training in breast cancer biology and to encourage the use of the powerful tools of contemporary molecular biology, genetics and chemistry to unravel the fundamental mechanisms of breast neoplasia.

On the face of it, recruitment of first and second year students would appear to be a sound policy for a new breast cancer graduate program; however, all graduate students at Northwestern University join a general education program with three rotations to laboratories on campus before they select a mentor at the end of the second year. If we committed our limited resources from the Army grant to first and second year students, the funds would primarily be used as university fees for a general pool of students with no commitment to breast cancer. Our goal is to enhance the education of students whose projects are related to breast cancer issues, and to provide a framework of knowledge about the clinical disease and the current scientific issues in the literature.

Two years ago, Northwestern made a commitment to develop a clinical and research breast cancer program. This goal has been achieved with the establishment of a breast cancer research core facility in the Robert H. Lurie Cancer Center by Dr. V. Craig Jordan and a clinical research program by Dr. Monica Morrow. These accomplishments in basic and clinical research provide the students on the breast cancer graduate training program with a new environment to learn and develop their skills. Since the training program cannot provide scholarships to entering students and support them through their 4-5 years as a graduate student, we have chosen to maximize our resources to encourage and develop those students who have already gained laboratory skills and wish to learn more about breast cancer. The students in years 3-5 are already gaining laboratory and research skills from their mentors and benefit the most from the weekly journal clubs. Dr. Jordan leads the discussion at the weekly meetings where a student presents a selected breast cancer topic from the basic and clinical literature. Although there are only four allocated positions available on the Army grant, the journal club attracts 10 - 20 graduate and postdoctoral participants (Appendix 1).

To reinforce the research program, Dr. Jordan has now established monthly breast cancer research meetings to bring together the diverse interests in breast cancer on the Northwestern campuses in Evanston and Chicago. At present, the meetings are monthly and the faculty review progress in their research on their breast cancer grants. The response to this new scientific meeting has been so exceptional that there are plans to make the meetings every two weeks. The graduate students on the Army training grant will also attend these research meetings.

In addition to laboratory training, the Breast Cancer Journal Club, and the newly established research meetings, students attended numerous seminars and journal clubs. These include the Tumor Cell Biology Seminar Series (Appendix 2), Cell and Molecular Biology Seminars, and exposure to a multidisciplinary management conference on breast cancer. In addition, during the past year there were two special seminars at the Lurie Cancer Center by distinguished investigators in the field of breast cancer biology (Appendix 3):

<u>Name</u>	<u>Title</u>
Neena Bissell, Ph.D.	Matrix Induction through Integrins
Katherine Horwitz, Ph.D.	Breast Cancer Molecular Mechanisms of Antagonist and Hormone Resistance

Students also attended the Coleman Symposium (September 18-19) on Regulation of Cell Growth (Appendix 4) and the Malnati Symposium (June 15-16) on Oncology: The Year in Review (Appendix 5).

Ten applications were submitted to the Advisory Committee for the Training Program for Year 1 funding:

Army Training Grant Applicants for Year 1 Funding:

<u>Name</u>	<u>Principal Investigator</u>	<u>Department</u>
S. Sundaresan	J. Larry Jameson, M.D., Ph.D.	Medicine
S-J Tzeng	Daniel Linzer, Ph.D.	BMBCB*
Shannon Hertler	Stephen Adam, Ph.D.	Cell & Molec Biology
Dave Dawson	Noel Bouck, Ph.D.	Micro/Immuno
Paul Gillis	Noel Bouck, Ph.D.	Micro/Immuno
Catherine Fillmore	Laurie Hudson, Ph.D.	Molec Pharm & Biol Chem
Sameer Mathur	Richard Morimoto, Ph.D.	BMBCB*
M. Shanmugam	Mary Hunzicker-Dunn, Ph.D.	Cell & Molec Biology
Puneet Opal	Robert Goldman, Ph.D.	Cell & Molec Biology
Julie McLachlan	Ouahid Bakouche, Ph.D.	Mole Pharm & Biol Chem

*BMBCB Biochemistry, Molecular Biology and Cell Biology

Four students were selected by the Training Grant Advisory Committee to receive funding for their research. Committee Members include: Christopher Bradfield, Ph.D., V. Craig Jordan, Ph.D., Steven T. Rosen, M.D., and Daniel Linzer, Ph.D.

1. Shiang-Jong Tzeng is a third year student working in the laboratory of Dr. Daniel Linzer in the Department of Biochemistry, Molecular Biology and Cell Biology. Mr. Tzeng is studying the function of the mammalian prolactin receptor. In the mouse, there are four prolactin receptors. These receptors differ only in their carboxy-terminal cytoplasmic domains. Since prolactin is one of the primary regulators of mammary gland development and function, an understanding of the mechanisms of action of the receptors for this hormone is central to an understanding of the abnormal mammary gland in breast cancer. Mr. Tzeng is focusing on the expression and function of the embryonic mouse prolactin receptors using PCR and in situ hybridization. These studies may reveal specific patterns of expression of the individual receptor forms and could help explain if aberrant expression of a predominantly fetal form of the prolactin receptor occurs in mammary carcinomas.

2. Malathy Shanmugam is a fourth year student in the laboratory of Dr. Mary Hunzicker-Dunn in the Cell and Molecular Biology Department. Previous work in Dr. Hunzicker-Dunn's laboratory has demonstrated that PKC δ is the isoform of protein kinase C that is upregulated in estrogen target tissues. PKC δ is also the predominant isoform in estrogen responsive MCF-7 breast cancer cells and is absent from estrogen unresponsive MBD-MB-231 cells. The goal of Ms. Shanmugam's research is to determine the role of PKC δ in hormone sensitive and hormone resistant breast cancer.

3. Sameer Mathur is a fourth year student in the laboratory of Richard Morimoto, Ph.D., Chairman, Biochemistry, Molecular Biology and Cell Biology. Mr. Mathur is studying a heat shock transcription factor, HSF2, which is a developmentally regulated factor. HSF2 is a key regulatory transcription factor for the molecular chaperones, HSP70 and HSP90, both of which are important regulatory proteins for estrogen, progesterone, and glucocorticoid receptors. These studies will provide new insights into the cooperative and synergistic regulatory interactions of heat shock proteins and hormone receptors mediated at the level of transcriptional control. These studies have a direct relationship to breast cancer, as deregulation of heat shock protein expression has been implicated in breast cancer.

4. Julie McLachlan is third year student in the laboratory of Ouahid Bakouche, Ph.D., Department of Molecular Pharmacology and Biological Chemistry. Dr. Bakouche has shown that monocytes isolated from aged individuals ("aged monocytes") are greatly deficient in their cytotoxic and tumoricidal abilities when compared to monocytes isolated from young individuals ("young monocytes"). Ms. McLachlan is investigating the biochemical, molecular and signal transduction differences between young and aged monocytes to explain the decreased efficiency of monocyte activation and cytotoxicity in the elderly. Monocytes/macrophages play a prominent role in host defense against breast

cancer. It is possible that decreased efficiency of monocytes may play a role in the incidence of breast cancer in the elderly.

In year 2 of the Training Grant there were 7 applicants:

<u>Name</u>	<u>Investigator</u>	<u>Department</u>
Ann Buchmann	Bayar Thimmapaya, Ph.D.	Micro/Immuno
Catherine Fillmore	Laurie Hudson, Ph.D.	Molec Pharm & Biol Chem
Stephanie Hsu	Noel Bouck, Ph.D.	Micro/Immuno
Richard Lee	Richard Pestell, Ph.D.	Medicine
Todd McAdams	Terry Papoutsakis, Ph.D. William Miller, Ph.D.	Chem Engineering
M. Shanmugam	Mary Hunzicker-Dunn, Ph.D.	Cell & Molec Biology
Gina Visser	Stephen Adam, Ph.D.	Cell & Molec Biology

Four students were selected by the Advisory Committee (same committee) to join the Training Grant Program:

1. Ann Buchmann is a fifth year student in the laboratory of Bayar Thimmapaya, Ph.D., Professor of Microbiology/Immunology. Dr. Thimmapaya is studying the molecular mechanisms of metalloprotease regulation and overexpression in tumor metastasis. He is also collaborating with Sigmund Weitzman, M.D., Professor of Medicine, on a project designing viral vectors with breast cell specific promoters to deliver suicide genes such as thymidine kinase and cytidine deaminase into breast cancer tissues. Ms Buchmann's research focuses on the cellular targets of the tumor suppressor gene product retinoblastoma. Retinoblastoma protein, pRb, controls the cell cycle by binding to and controlling various cellular genes whose actions are necessary for progression into the S phase of the cell cycle. Mutations of pRb or deletion of the Rb gene has been seen in several types of tumors, including 20-30% of breast tumors. Ms. Buchmann is trying to elucidate the path by which Rb controls cell cycle progression and tumorigenesis by identifying and studying genes that are transcriptionally controlled by pRb. She has constructed an adenovirus vector that overexpresses pRb, has shown that the protein produced by this virus acts normally in the cell, and has developed a system to infect a population of synchronized cells which overexpress the Rb gene. She is now

identifying genes controlled by pRb and will then look at expression of these genes in breast tissue to see whether they are amplified.

2. Stephanie Hsu is a fourth year student in the laboratory of Noel Bouck, Ph.D., Professor of Microbiology/Immunology. Dr. Bouck is studying the angiogenic factor thrombospondin, a multifunctional adhesion protein that is produced by normal breast epithelial cells and is a potent inhibitor of neovascularization in vivo. Dr. Bouck has shown that thrombospondin is regulated by the p53 tumor suppressor gene in a breast carcinoma cell line. Wild-type p53 expression is often lost during breast tumor progression. When p53 was re-introduced into a breast cancer cell line containing only mutant p53, revertants began to produce thrombospondin which was responsible for shifting their angiogenic phenotype from inducing to inhibitory. Ms Hsu is looking at the role of thrombospondin in the progression of glioblastoma multiforme. Normal astrocytes produce thrombospondin, but its expression is lost as cells become invasive and malignant. Ms. Hsu has linked this loss to a loss of a tumor suppressor gene on chromosome 10, since re-introduction of a normal copy of chromosome 10 into glioblastoma cell lines consistently reverted to tumorigenicity and shifted the cells to an angioinhibitory phenotype due to an upregulated thrombospondin production. Genetic instability at chromosome 10 has also been observed in primary breast tumors, suggesting that thrombospondin may be regulated by similar mechanisms in both tumors. Aims of the current research include determining the importance of thrombospondin in tumor formation, understanding its regulation and identifying other factors involved in the angiogenic phenotype.

3. Todd McAdams is a fourth year student in the laboratories of Drs. Terry Papoutsakis, Professor, Chemical Engineering and William Miller, Associate Professor, Chemical Engineering. Clinical trials of high-dose chemotherapy in conjunction with peripheral blood stem cell (PBSC) transplantation for breast cancer patients has higher response rates than conventional chemotherapy. The presence of tumor cells in the peripheral blood necessitates purging prior to transplant. One serious drawback to purging, however, is that agents used to eliminate rapidly dividing tumor cells also eliminate rapidly dividing hematopoietic progenitors. One potential solution to this problem is the use cytokine assisted ex vivo expansion of peripheral blood stem cells following elimination of tumor cells. Drs. Papoutsakis and Miller have developed a perfusion reactor system for large scale expansion of hematopoietic cultures. Todd McAdams' project involves optimization of culture pH and the engineering of growth factor tethered surfaces for improving the expansion of peripheral blood stem cells from breast cancer patients. Mr. McAdams has used a combination of colony assays, flow cytometry and histological staining to show that erythroid differentiation is blocked at low pH and enhanced at high pH. He is currently examining the associated changes in erythroid gene expression. Mr. McAdams is also investigating how hemtopoietic cells respond to cytokines bound to the culture

substrate rather than free in solution. It is hoped that bound cytokines in serum free media will lead to increased hematopoietic culture proliferation, the directing of stem cells into specific lineages, and reduced growth factor requirements.

4. Malathy Shanmugam, a fifth year student, received a second year of funding for her work in the laboratory of Dr. Mary Hunzicker-Dunn, Professor, Cell and Molecular Biology. Ms. Shanmugam has demonstrated that PKC δ is the predominant PKC isoform in estrogen responsive MCF-7 cells and is present, but in a catalytically inactive conformation in estrogen unresponsive MDA-MB-231 cells. The laboratory has demonstrated that HSP27 is the PKC- δ substrate. The hypothesis, therefore, is that PKC- δ in its active conformation limits the rate of cellular proliferation in estrogen responsive breast cancer cells through phosphorylation of substrates including HSP27. Estrogen's enhancement of proliferation in estrogen receptor positive breast cancer cells is linked in part to a reduction in PKC δ protein; and that the more aggressive phenotype of estrogen receptor negative breast cancer cells results in part from the absence of catalytically active PKC- δ . In this second year of funding, Ms. Shanmugam will directly test the effect of PKC δ on the growth of MCF-7 cells by transfecting these cells with constitutively active and dominant negative PKC - δ constructs and evaluating the cells growth responses as well as phosphorylation of HSP27. The prediction is that estrogen will no longer be able to enhance proliferation of MCF-7 cells expressing constitutively active PKC - δ .

In June 1995, the Cancer Center applied for a supplement to the Training Grant through the National Action Plan on Breast Cancer (NAPBC), Public Health Service's Office on Women's Health. The Center just received notification of an award for one post-doctoral position per year for a total of three years. The U.S. Army Medical Research and Materiel Command awards and administers the funds. A solicitation to all investigators in the Training Grant Program will be sent out immediately to fill the position. A candidate will be selected by the Training Grant Advisory Committee by November 15, 1995. The fellow will participate in the Breast Cancer Journal Club weekly meetings.

CONCLUSIONS

Overall, the new breast cancer program at the Robert H. Lurie Cancer Center now provides an exceptional environment to develop the research potential of committed individuals. There is an enormous level of interest in the field of breast cancer as evidenced by the number of applicants applying for funding. Our focus is to attract talented students interested in conducting research in breast cancer, but who would not have this potential enhanced without our program and to lay the foundation for training individuals to be recruited as postdoctoral fellows in other centers of excellence. We feel strongly that our research based program will enhance the future pool of trained individuals to contribute actively to breast cancer related problems. The process for selection of students by the Training Grant Advisory Committee has run smoothly.

Students who were selected to the Program in Year 1 participated in the Breast Cancer Journal Club and seminars on a regular basis. A schedule for the coming year has been made which includes the Year 2 students. One new post-doctoral fellow will be selected to fill the position made available by supplemental funds.

Breast Cancer Program Journal Club

The Breast Cancer Program Journal Club will be held on Tuesdays at 11:00 in Vanderwicken Library, room 8261, Olson Pavilion, beginning October 3, 1995. Please see the attached schedule.

The presenter should submit three papers at least two weeks prior to their scheduled presentation to either Dr. Jordan or Dr. Tonetti for approval, and should distribute the paper to all members the week before. Each member of the Journal Club should have read the paper thoroughly and be prepared to participate in a discussion. The presenter will be expected to prepare appropriate transparencies necessary to explain any pertinent background information that is relevant to the subject of the paper. The purpose of the paper should be clearly defined and the presenter should be able to explain any of the methods used in the experimental design. All data from the paper should be displayed on a transparency (enlarged for optimal viewing) so that the group can discuss the results. The presenter should enumerate the conclusions the authors have stated in the paper and discuss the legitimacy (or lack thereof) based on the data presented in the paper.

The Breast Cancer Program graduate students must present at least one paper during the semester and must attend the Journal Club every week. Some of the topics that are appropriate for the Journal Club are as follows:

- Clinical aspects of hormones and breast cancer
- Cell Biology of estrogen receptors/antiestrogens
- Metabolism of antiestrogens and carcinogenesis
- Animal models of breast cancer

If you have any questions please contact Dr. Debra Tonetti, (312) 908-7301 or (312) 908-9798, Olson Pavilion, 8307.

BREAST CANCER PROGRAM JOURNAL CLUB

October 3	Dr. V. Craig Jordan
October 10	Dr. Debra Tonetti
October 17	Dr. Malcolm Bilimoria
October 24	Dr. Zehan Chen
October 31	Sameer Mathur
November 7	Dr. Marc Lippman (outside invited speaker)
November 14	Shiang-Jong Tzeng
November 21	Dr. Marco Gottardis (outside invited speaker)
November 28	Shannon Hackett
December 5	Dr. Ana Levenson
December 12	Dr. Vasilis Assikis
December 19	Stephanie Hsu
January 9	Todd McAdams
January 16	Ann Buchman

Breast Cancer Program Journal Club

The Breast Cancer Program Journal Club will be held on Tuesdays at 11:00 in Vanderwicken Library, room 8261, Olson Pavilion, beginning January 3, 1995. A paper will be assigned to each presenter and will be distributed to the other members of the Journal Club at least one week before the scheduled presentation. Each member of the Journal Club should have read the paper thoroughly and be prepared to participate in a discussion.

The presenter will be expected to prepare appropriate transparencies necessary to explain any pertinent background information that is relevant to the subject of the paper. The purpose of the paper should be clearly defined and the presenter should be able to explain any of the methods used in the experimental design. All data from the paper should be displayed on a transparency (enlarged for optimal viewing) so that the group can discuss the results. The presenter should enumerate the conclusions the authors have stated in the paper and discuss the legitimacy (or lack thereof) based on the data presented in the paper.

The Breast Cancer Program graduate students must present at least one paper during the semester and must attend the Journal Club at least once per month. The topics that the Journal Club will focus on during the first few months will be as follows:

- Clinical aspects of hormones and breast cancer
- Cell Biology of estrogen receptors/antiestrogens
- Metabolism of antiestrogens and carcinogenesis
- Animal models of breast cancer

BREAST CANCER PROGRAM JOURNAL CLUB

January 10 Dr. Craig Jordan

Weckbecker et al. Somatostatin Analogue Octreotide Enhances the Antineoplastic Effects of Tamoxifen and Ovariectomy on 7,12-Dimethylbenz(a)anthracene-induced Rat Mammary Carcinomas. *Cancer Research* 54:6334-6337, 1994.

January 17 Dr. Claudia Tellez

DeFriend, D.J., Howell, A, Nicholson, RI, Anderson E., Dowsett, M, Mansel RE, Blamey RW, Bundred, NJ, Robertson JF, Saunders C, Baum, M, Walton P, Sutcliff F, and Wakeling A. Investigation of a New Pure Antiestrogen (ICI 182789) in Women with Primary Breast Cancer. *Cancer Research* 54:408-414, 1994.

January 24 Dr. Ana Levenson

Lykkesfeldt, AE, Madson MW and Briand P. Altered Expression of Estrogen-regulated Genes in a Tamoxifen-resistant ICI 182,780 Sensitive Human Breast Cancer Cell Line, MCF-7/TAM^R-1. *Cancer Research* 54:1587-1595, 1994.

January 31 Dr. Malcolm Bilimoria

Anzano, MA, Byers SW, Smith JM, Peer CW, Mullen LT, Brown CC, Roberts AB and Sporn MB. Prevention of Breast Cancer in the Rat with 9-*cis*-Retinoic Acid as a Single Agent and in Combination with Tamoxifen. *Cancer Research* 54:4614-4617, 1994.

February 7 Sameer Mathur

To Be Announced

February 14 Dr. Debra Tonetti

Yue W, Zhou D, Chen S and Brodie A. A New Nude Mouse Model for Postmenopausal Breast Cancer Using MCF-7 Cells Transfected with the Human Aromatase Gene. *Cancer Research* 54:5092-5095, 1994.

February 21 Dr. Vasilis Assikis

Ito K, Watanabe K, Nasim S, Sasano H, Sato S, Kyajima A, Silverberg SG and Garret CT. Prognostic Significance of p53 Overexpression in Endometrial Cancer. *Cancer Research* 54:4667-4670, 1994.

February 28 Dr. Craig Jordan

Vancutsem, PM, Lazarus, P and Williams GM. Frequent and Specific Mutations of the Rat p53 Gene in Hepatocarcinomas Induced by Tamoxifen. *Cancer Research* 54:3864-3867, 1994.

March 7 Malathy Shanmugan

To Be Announced

March 14 Dr. Ana Levenson

Phillips DH, Carmichael PL, Hewer A, Cole KJ and Poon GK. *a*-Hydroxytamoxifen, a Metabolite of Tamoxifen with Exceptionally High DNA-binding Activity in Rat Hepatocytes. *Cancer Research* 54:5518-5522, 1994.

March 21 Dr. Malcolm Bilimoria

Schoenfeld A, Luqmani Y, Smith D, O'Reilly S, Shousha S, Sinnott HD, and Coombes RC. Detection of Breast Cancer Micrometastases in Axillary Lymph Nodes by Using Polymerase Chain Reaction 54:2986-2990, 1994.

March 28 Julie McLachlon

To Be Announced

April 4 Dr. Debra Tonetti

Wei, LL and Miner R. Evidence for the Existence of a Third Progesterone Receptor Protein in Human Breast Cancer Cell Line T47D. *Cancer Research* 54:340-343, 1994.

April 11 Dr. Claudia Tellez

Fabian CJ, Kimler BF, McKittrick R, Park CH, Lin F, Krishan L, Jewell WR, Osborne CK, Martino S, Hutchins LF, Leong SA and Green S. Recruitment with High Physiological Doses of Estradiol Preceding Chemotherapy: Flow Cytometric and Therapeutic Results in Women and Locally Advanced Breast Cancer - A Southwest Oncology Group Study. *Cancer Research* 54:5357-5362, 1994.

April 18 Shiang-Jong

To Be Announced

APPENDIX 2
DEPARTMENT OF PATHOLOGY AND THE ROBERT H. LURIE CANCER CENTER
TUMOR CELL BIOLOGY AND CARCINOGENESIS SEMINARS

THURSDAYS **VANDERWICKEN LIBRARY** **OLSON 8260** **1:00 P.M.-2:00 P.M.**

WINTER 1996

January 4	NEW YEAR
January 11	<i>Lou Laimins, Associate Professor</i> Department of Microbiology-Immunology Modulation of Epithelial Differentiation by Human Papilloma Virus
January 18	<i>Stephen Adam, Associate Professor</i> Cell and Molecular Biology Cytoplasmic Factors in Nuclear Protein Import
January 25	<i>Frank E. McDonald, Assistant Professor</i> Department of Chemistry New Strategies for the Chemical Synthesis of Antitumor Principles
February 1	<i>Masato Okamoto, Research Associate</i> Department of Pathology In Vitro Urinary Bladder Carcinogenesis by Hydrogen Peroxide and Interleukin 6
February 8	<i>Jeffrey Ny, Associate Professor</i> Molecular Pharmacology and Biological Chemistry Role of Notch Signaling in Mammalian Neurogenesis
February 15	<i>Jeff Kuret, Associate Professor</i> Molecular Pharmacology and Biological Chemistry The Structural Basis of Protein Kinase Substrate and Inhibitor Selectivity
February 22	<i>Gerald Soff, Associate Professor</i> Department of Medicine Angiostatin Production by Human Prostate Carcinoma
February 29	<i>Grant Kraft, Assistant Professor</i> Molecular Pharmacology and Biological Chemistry TBA
March 7	<i>Benette Phillips, Assistant Professor</i> Departments of Obstetrics/Gynecology and Cell and Molecular Biology Methylation-Associated Gene Silencing
March 14	TBA
March 21	<i>Andrew Andres, Assistant Professor</i> Molecular Pharmacology and Biological Chemistry Steroid Regulation of Insect Development: A Molecular/Genetic Analysis of E63-1, a Primary-Response Gene Required for Drosophila Molting
March 28	TBA

**CENTER FOR REPRODUCTIVE
SCIENCE**

P-30 CENTER CONSULTANT

**KATHYRN B. HORWITZ, PHD
DEPARTMENT OF MEDICINE
UNIVERSITY OF COLORADO HEALTH SCIENCE
CENTER**

**BREAST CANCER MOLECULAR MECHANISMS OF
ANTAGONIST AND HORMONE RESISTANCE**

**4:00 PM
MONDAY, APRIL 03, 1995
F. Searle Building 3-417
Northwestern University, Evanston
Sponsored by P-30 CENTER Grant**

HORWITZ.GEM

APPENDIX 4

The Robert H. Lurie Cancer Center of Northwestern University presents

The Coleman Foundation Symposium

The Regulation of Cell Growth

Monday September 18, 1995

8:00 a.m.
Registration and continental breakfast

8:30 a.m.
Morning Session

Welcome

Dr. Steven T. Rosen
Director
The Robert H. Lurie Cancer Center of Northwestern University

Scott Ness, PhD
Symposium Organizer
Department of Biochemistry, Molecular Biology, and Cell Biology
Northwestern University

Receptors and Signals

Introduction and Overview

Scott Ness
Northwestern University
Session Chair

Signal Transduction by the PDGF Receptor

Andrius Kazlauskas
National Jewish Center
Denver

Registration

The Regulation of Cell Growth

The Coleman Foundation Symposium sponsored by The Robert H. Lurie Cancer Center of Northwestern University

Monday and Tuesday September 18 and 19, 1995

Northwestern University
Norris University Center
1999 North Campus Drive
Evanston, Illinois

Registration information

Full fee is \$60.00. The fee for postdoctoral trainees is \$35.00, and for students, \$25.00. **Postdoctoral trainees and students who send**

poster session information by Friday, August 18, 1995, may register at a reduced rate of \$25.00 (postdoctoral trainees) or \$15.00 (students). When sending registration, trainees and students must include an accompanying letter confirming their status from a program director or faculty advisor. **Please make checks payable to the Robert H. Lurie Cancer Center.** To register, please mail this panel with the registration fee to

The Robert H. Lurie Cancer Center of Northwestern University
Olson 8250 N505
303 East Chicago Avenue
Chicago, Illinois 60611-3008
Tel.: 312.908.5258
Fax: 312.908.1372
E-mail: rky@merle.acns.nwu.edu

Name _____

Title/Position _____

Department _____

Institution _____

Street Address _____

City/State/Zip _____

Daytime phone _____

Daytime fax _____

E-mail _____

Registration fee enclosed \$ _____

I am a student or postdoctoral trainee. A letter from my program director or faculty advisor confirming my status is enclosed. ☐ yes

I plan to participate in the Symposium poster session.
An abstract is enclosed. ☐ yes

I am not affiliated with Northwestern University and will need parking; please contact me and provide information. ☐ yes

APPENDIX 5

Thursday, June 15, 1995

7:30 a.m. Registration and continental breakfast

8:15 a.m. Introduction

Steven T. Rosen, MD, FACP
Director
The Robert H. Lurie
Cancer Center
of Northwestern University

8:30 a.m. Breast Cancer

Moderator
William J. Gradishar, MD
Department of Medicine
Division of Hematology-Oncology

Surgery
Monica Morrow, MD
Department of Surgery
Director, Clinical Breast Cancer
Program
Northwestern Memorial Hospital

Radiation Oncology
Krystyna D. Kiel, MD
Department of Radiology
Division of Radiation Oncology

Medical Oncology
Douglas E. Merkel, MD
Department of Medicine
Division of Hematology-Oncology

Panel Discussion

10:00 a.m. Gastrointestinal Oncology

Moderator
Al B. Benson III, MD
Department of Medicine
Division of Hematology-Oncology

Surgery
Mark S. Talamonti, MD
Department of Surgery

Radiation Oncology
William Bloomer, MD
Department of Radiology
Chief of Radiation Oncology
Evanston Hospital Corporation

Medical Oncology
Gershon Y. Locker, MD
Department of Medicine
Division of Hematology-Oncology

Panel Discussion

11:30 a.m. to 1:00 p.m. Lunch break

1:00 p.m. Genitourinary Oncology

Moderator
Janardan D. Khandekar, MD
Department of Medicine
Chief of Hematology-Oncology
Evanston Hospital Corporation

Surgery
James M. Kozlowski, MD
Departments of Urology and
Surgery
Division of Urologic Oncology

Radiation Oncology
Ramananda M. Shetty, MD
Department of Radiology
Division of Radiation Oncology

Medical Oncology
Daniel H. Shevrin, MD
Department of Medicine
Division of Hematology-Oncology

Panel Discussion

2:30 p.m. Gynecologic Oncology

Moderator
John R. Lurain II, MD
Department of Obstetrics and
Gynecology
Chief, Division of Gynecologic
Oncology

Registration Oncology: The Year in Review

The Sixth Annual Malnati Symposium presented by The Robert H. Lurie Cancer Center of Northwestern University

Thursday and Friday June 15 and 16, 1995

Sponsored by Northwestern University Medical School Chicago, Illinois

Registration fees: full fee: \$100.00; residents and fellows, \$50.00. All residents and fellows, including those associated with Northwestern University, must provide written verification of their status from a program director or faculty advisor. Please make checks payable to Northwestern University Medical School.

To register, please return this panel with the registration fee to

Northwestern University Medical School
Office of Continuing Medical Education
Ward Building 1-004 W111
303 East Chicago Avenue
Chicago, Illinois 60611-3008
Tel.: 312.503.8533 Fax: 312.503.0146

Name _____	Degree _____
Department and/or title _____	
Institution _____	
Street Address _____	
City _____	State/Zip _____
Work Area Code/Telephone _____	
Social Security Number (for CME records) _____	
Certification of status as resident or fellow is enclosed. <input type="checkbox"/> yes	
Signature _____	